01B09-5

PLASMA KINETICS OF METHIONINE-HOMOCYSTEINE IN STREPTOZOTOCIN-INDUCED DIABETIC RATS
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An elevated plasma homocysteine level is considered as an independent risk factor for cardiovascular disease. Homocysteine is formed from methionine through the intermediate S-adenosylmethionine. Homocysteine is then metabolized by remethylation and transsulfuration. Cardiovascular disease is a major complication of diabetes. However, diabetic patients without kidney dysfunction have decreased plasma homocysteine levels. The reason for such decreased homocysteine levels is unknown. The purpose of this study was to investigate the plasma kinetics of methionine-homocysteine in a type 1 diabetic animal model. Diabetes was induced by intraperitoneal injection of streptozotocin to S.D. rats. After intravenous administration of [3H]methionine or [3H]methionine into the diabetic and control rats, the plasma concentrations of [3H]methionine, [3H]methionine and [3H]homocysteine were determined simultaneously with endogenous methionine and homocysteine by gas chromatography-mass spectrometry-selected ion monitoring. Endogenous plasma levels of the total homocysteine in the diabetic rats were significantly lower than those in the control rats. The total plasma clearance of [3H]methionine was not significantly different between the diabetic and control rats. The AUC values of total [3H]homocysteine and [3H]methionine in the diabetic rats decreased in comparison with those in the control rats. After administration of [3H]methionine, the AUC values of total [3H]homocysteine also decreased in the diabetic rats. The metabolic clearance associated with conversion of [3H]methionine into [3H]methionine in the diabetic rats was about 30% lower than that in the controls, suggested that a diabetic state appears to be a diminished transmethylation flux.

01B10-1

ENHANCED RENAL ACCUMULATION OF CISPLATIN DETERIORATES ACUTE KIDNEY INJURY IN HYPOMAGNESEMIC RATS
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Hypomagnesemia has emerged as a common event associated with cisplatin-induced acute kidney injury (AKI). However, there is a paucity of information concerning the pathogenesis and mechanisms underlying cisplatin-associated hypomagnesemia and the associated kidney damage. Here, we investigated that the effect of dietary magnesium (Mg) on the pharmacokinetics of cisplatin. Rats fed an adequate diet containing Mg (3.5g/kg) (control group) or Mg-deficient diet (low Mg group) from 7 days before intraperitoneal or intravenous administration of cisplatin. The amount of platinum (Pt) was determined using inductively coupled plasma-mass spectrometry. The serum Mg level and body weight of low Mg group decreased compared to control group. Hypomagnesemic rats treated with cisplatin displayed markedly elevations of serum BUN and creatinine. Plasma concentration profile of Pt after the administration of cisplatin in hypomagnesemic rats was not significantly differed compared to that in control rats. Mg-deficient diet had no significant effect on the concentration of Pt in the liver and lung at 24 and 168 hr after the administration of cisplatin. In contrast, the concentration of Pt in the kidney was about 2-fold higher in hypomagnesemic rats compared to that in the kidney of control rats at 24 and 168 hr. Furthermore, The Kp value in the kidney at 168 hr after administration of cisplatin in control and low Mg group were about 2 and 4-fold greater than that at 24 hr, respectively. These results suggest that hypomagnesemia stimulates cisplatin transport activity in basolateral and/or apical membranes of renal tubular cells. In conclusion, hypomagnesemia enhanced the development of cisplatin-induced AKI, which was caused by the increased renal accumulation of cisplatin.